Amendments to the Claims

This listing of claims replaces all prior versions and listings of claims in the application.

Listing of Claims

1-36. (Canceled)

37. (New) A conjugate of hydroxyalkylstarch and a low molecular weight substance, characterized in that the binding interaction between the hydroxyalkylstarch molecule and the low molecular weight substance is based on a covalent bonding which is the result of a coupling reaction between (i) the terminal aldehyde group, or a functional group derived from this aldehyde group by chemical reaction, of the hydroxyalkylstarch molecule and (ii) a functional group, which is able to react with this aldehyde group or functional group derived therefrom of the hydroxyalkylstarch molecule, of the low molecular weight substance, where the bonding resulting directly in the coupling reaction can be modified where appropriate by a further reaction to give the abovementioned covalent bonding.

38. (New) The conjugate as claimed in claim 37, characterized in that the functional group derived from the terminal aldehyde group of the hydroxyalkylstarch molecule is one of the functional groups of a bifunctional linker molecule with which the terminal aldhehyde group or a functional group derived therefrom has been reacted.

39. (New) The conjugate as claimed in claim 37, characterized in that the reactive functional group of the low molecular weight substance is one of the functional groups of a bifunctional linker molecule which has been coupled to the low molecular weight substance.

40. (New) The conjugate as claimed in claim 37, characterized in that the covalent bonding is the result of a coupling reaction between a carboxyl group formed by selective oxidation of the terminal aldehyde group of the hydroxyalkylstarch molecule, or activated carboxyl group, and a primary amino group or thiol group of the low molecular weight substance.

41. (New) The conjugate as claimed in claim 40, characterized in that the covalent bonding is an amide linkage which is the result of a coupling reaction between a lactone formed by selective oxidation of the terminal aldehyde group of the hydroxyalkylstarch molecule, and a primary amino group of the low molecular weight substance.

42. (New) The conjugate as claimed in claim 37, characterized in that the covalent bonding is an amine linkage which is the result of a coupling reaction between the terminal aldehyde group of the hydroxyalkylstarch molecule and a primary amino group of the low molecular weight substance to form a Schiff's base, and reduction of the Schiff's base to the amine.

43. (New) The conjugate as claimed in claim 37, characterized in that the hydroxyalkylstarch molecule has a molecular weight in the range from about 70 to about 1000 kD.

44. (New) The conjugate as claimed in claim 43, characterized in that the hydroxyalkylstarch molecule has a molecular weight of about 130 kD.

45. (New) The conjugate as claimed in claim 37, characterized in that the hydroxyalkylstarch molecule has a degree of substitution of from about 0.3 to about 0.7.

46. (New) The conjugate as claimed in claim 37, characterized in that the hydroxyalkylstarch molecule has a ratio of C_2 to C_6 substitution of from 8 to 12.

47. (New) The conjugate as claimed in claim 37, characterized in that the hydroxyalkylstarch molecule is a hydroxyethylstarch molecule.

48. (New) The conjugate as claimed in claim 37, characterized in that the low molecular weight substance is an active pharmaceutical ingredient.

49. (New) The conjugate as claimed in claim 48, characterized in that the active

pharmaceutical ingredient is selected from the group composed of antibiotics, antidepressants, antidiabetics, antidiuretics, anticholinergics, antiarrhythmics, antiemetics, antiepileptics, antihistamines, antimycotics, antisympathotonics, antithrombotics, androgens, antiandrogens, estrogens, antiestrogens, antiosteoporotics, antitumor agents, vasodilators, other antihypertensive agents, antipyretic agents, analgesics, antiinflammatory agents, β-blockers, immunosuppressants and vitamins.

50. (New) The conjugate as claimed in claim 48, characterized in that the functional group of the active pharmaceutical ingredient involved in the coupling reaction is an amino group.

51. (New) The conjugate as claimed in claim 50, characterized in that the active pharmaceutical ingredient is selected from the group composed of albuterol, alendronate, amikazin, aminopenicillin, amoxicillin, atenolol, azathioprine, cefaclor, cefadroxil, cefotaxime, ceftazidime, ceftriaxone, cilastatin, cimetidine, ciprofloxacin, clonidine, colistin, cosyntropin, cycloserine, daunorubicin, doxorubicin, desmopressin, dihydroergotamine, dobutamine, dopamine, ephedrine, epinephrine, ε-aminocaproic acid, ergometrine, esmolol, famotidine, flecainide, folic acid, flucytosine, furosemide, ganciclovir, gentamicin, glucagon, hydrazaline, imipenem, isoproterenol, ketamine, liothyronine, LHRH, merpatricin, metaraminol, methyldopa, metoclopramide, metoprolol, mexiletine, mitomycin, neomycin, netilmicin, nimodipine, nystatin, octreotide, oxytocin, pamidronate, pentamidine, phentolamine, phenylephrine, procainamide, procaine, propranolol, ritodrine, sotalol, teicoplanin, terbutaline, thiamine, tiludronate, tolazoline, trimethoprim, tromethamine, vancomycin, vasopressin and vinblastine.

52. (New) The conjugate as claimed in claim 48, characterized in that the functional group of the active pharmaceutical ingredient involved in the coupling reaction is a carboxyl group or activated carboxyl group.

53. (New) The conjugate as claimed in claim 52, characterized in that the active pharmaceutical ingredient is selected from the group composed of acetylcysteine, azlocillin,

aztreonam, benzylpenicillin, camptothecin, cefamandole, cefazolin, cefepime, cefotaxime, cefotetan, cefoxitin, ceftazidime, ceftriaxone, cephalothin, cilastatin, ciprofloxacin, clavulanic acid, dicloxacillin, ε-aminocaproic acid, floxacillin, folinic acid, furosemide, fusidic acid, imipemem, indomethacin, ketorolac, liothyronine, melphalan, methyldopa, piperacillin, prostacyclin, prostaglandins, teicoplanin, ticarcillin and vancomycin.

54. (New) The conjugate as claimed in claim 48, characterized in that the functional group of the active pharmaceutical ingredient involved in the coupling reaction is an aliphatic or aryl-OH group.

55. (New) The conjugate as claimed in claim 54, characterized in that the active pharmaceutical ingredient is selected from the group composed of albuterol, allopurinol, apomorphine, ceftriaxone, dobutamine, dopamine, doxycycline, edrophonium, isoproterenol, liothyronine, metaraminol, methyldopa, minocycline, palcitaxel, pentazocine, phenylephrine, phentolamine, propofol, rifamycins, ritodrine, Taxol, teicoplanin, terbutaline, tetracycline and vancomycin.

56. (New) A pharmaceutical composition comprising an effective amount of a conjugate as claimed in claim 48 and a pharmaceutically acceptable carrier and, where appropriate, further excipients and active ingredients.

57. (New) The use of a conjugate as claimed in claim 48 for the therapeutic or preventative treatment of humans or animals.

58. (New) The use of a composition as claimed in claim 56 for the therapeutic or preventative treatment of humans or animals.

59. (New) A method for preparing a hydroxyalkylstarch conjugate as claimed in claim 37, characterized in that a coupling reaction is carried out between the terminal aldehyde group, or a

functional group derived from this aldehyde group by chemical reaction, of the hydroxyalkylstarch molecule and a functional group, able to react with this aldehyde group or functional group derived therefrom of the hydroxyalkylstarch molecule, of the low molecular weight substance, and where the bonding resulting directly in the coupling reaction is modified where appropriate by a further reaction.

60. (New) The method as claimed in claim 59, characterized in that the terminal aldehyde group of the hydroxyalkylstarch molecule is converted by selective oxidation into the corresponding lactone group, and the latter is subsequently reacted with a primary amino group of the low molecular weight substance so that the hydroxyalkylstarch molecule is linked to the low molecular weight substance by an amide linkage.

61. (New) The method as claimed in claim 60, characterized in that the selective oxidation of the aldehyde group is carried out with iodine or metal ions in basic aqueous solution.

62. (New) The method as claimed in claim 60, characterized in that the coupling reaction is carried out in the presence of carbodiimide, preferably 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide (EDC).

63. (New) The method as claimed in claim 59, characterized in that the coupling reaction is carried out in heterogeneous phase.

64. (New) The method as claimed in claim 59, characterized in that the coupling reaction is carried out in homogeneous phase in DMSO or N-methylpyrrolidone or glycol.

65. (New) The method as claimed in claim 59, characterized in that the coupling reaction is carried out in DMSO or N-methylpyrrolidone or glycol in the absence of an activator.

66. (New) The method as claimed in claim 59, characterized in that the terminal aldehyde group of the hydroxyalkylstarch molecule is coupled to a primary amino group of the low

molecular weight substance to form a Schiff's base, and the Schiff's base which has formed is reduced to the amine, so that the hydroxyethylstarch molecule is linked by an amine linkage to the low molecular weight substance.

67. (New) The method as claimed in claim 66, characterized in that the reducing agent is sodium borohydride, sodium cyanoborohydride or an organic boron complex.

68. (New) A method for preparing hydroxyalkylstarch which is selectively oxidized at the terminal aldehyde group, characterized in that the hydroxyalkylstarch is reacted in a molar ratio of iodine to HAS of 2:1 to 20:1 in basic aqueous solution.

69. (New) The method as claimed in claim 68, characterized in that the molar ratio of iodine to HAS is about 5:1 to 6:1.

70. (New) The method as claimed in claim 68, characterized in that

a) an amount of hydroxyalkylstarch is dissolved in hot distilled water, and somewhat less than 1 mole equivalent of aqueous iodine solution is added,

b) NaOH solution in a molar concentration which is about 5-15 times that of the iodine solution is slowly added dropwise at intervals of a plurality of minutes to the reaction solution until the solution starts to become clear again after the addition,

c) again somewhat less than 1 mole equivalent of aqueous iodine solution is added to the reaction solution,

d) the dropwise addition of the NaOH solution is resumed,

e) steps b) to d) are repeated until about 5.5-6 mole equivalents of iodine solution and 11-12 mole equivalents of NaOH solution, based on the hydroxyalkylstarch, have been added,

f) the reaction is then stopped and the reaction solution is desalted and subjected to a cation exchange chromatography, and the reaction product is obtained by lyophilization.

71. (New) The method as claimed in claim 70, characterized in that the aqueous iodine

solution is an approximately 0.05-0.5N iodine solution.

72. (New) The method as claimed in claim 70, characterized in that the molar concentration of the NaOH solution is about 10 times that of the iodine solution.

73. (New) A method for preparing hydroxyalkylstarch which is selectively oxidized at the terminal aldehyde group, characterized in that the HAS is oxidized in aqueous alkaline solution with a molar excess of stabilized metal ions selected from Cu^{2+} ions and Ag^{+} ions.

74. (New) A conjugate of hydroxyalkylstarch and a low molecular weight substance, wherein the binding interaction between the hydroxyalkylstarch molecule and the low molecular weight substance comprises at least one covalent bond between:

(i) the terminal aldehyde group of the hydroxyalkylstarch molecule, or a functional group derived from the terminal aldehyde group, and

(ii) a functional group of the low molecular weight substance.

75. (New) The conjugate of claim 74, wherein the functional group derived from the terminal aldehyde group of the hydroxyalkylstarch molecule is a functional group of a bifunctional linker coupled to the terminal aldhehyde group or functional group derived therefrom.

76. (New) The conjugate of claim 74, wherein the functional group of the low molecular weight substance is a functional group of a bifunctional linker coupled to the low molecular weight substance.

77. (New) The conjugate of claim 74, wherein the hydroxyalkylstarch molecule has a degree of substitution of from about 0.3 to about 0.7.

78. (New) The conjugate of claim 74, wherein the hydroxyalkylstarch molecule is a hydroxyethylstarch molecule.